

## Optimization of Solvent Drying ProMaxion for Dryer End-Point Detection

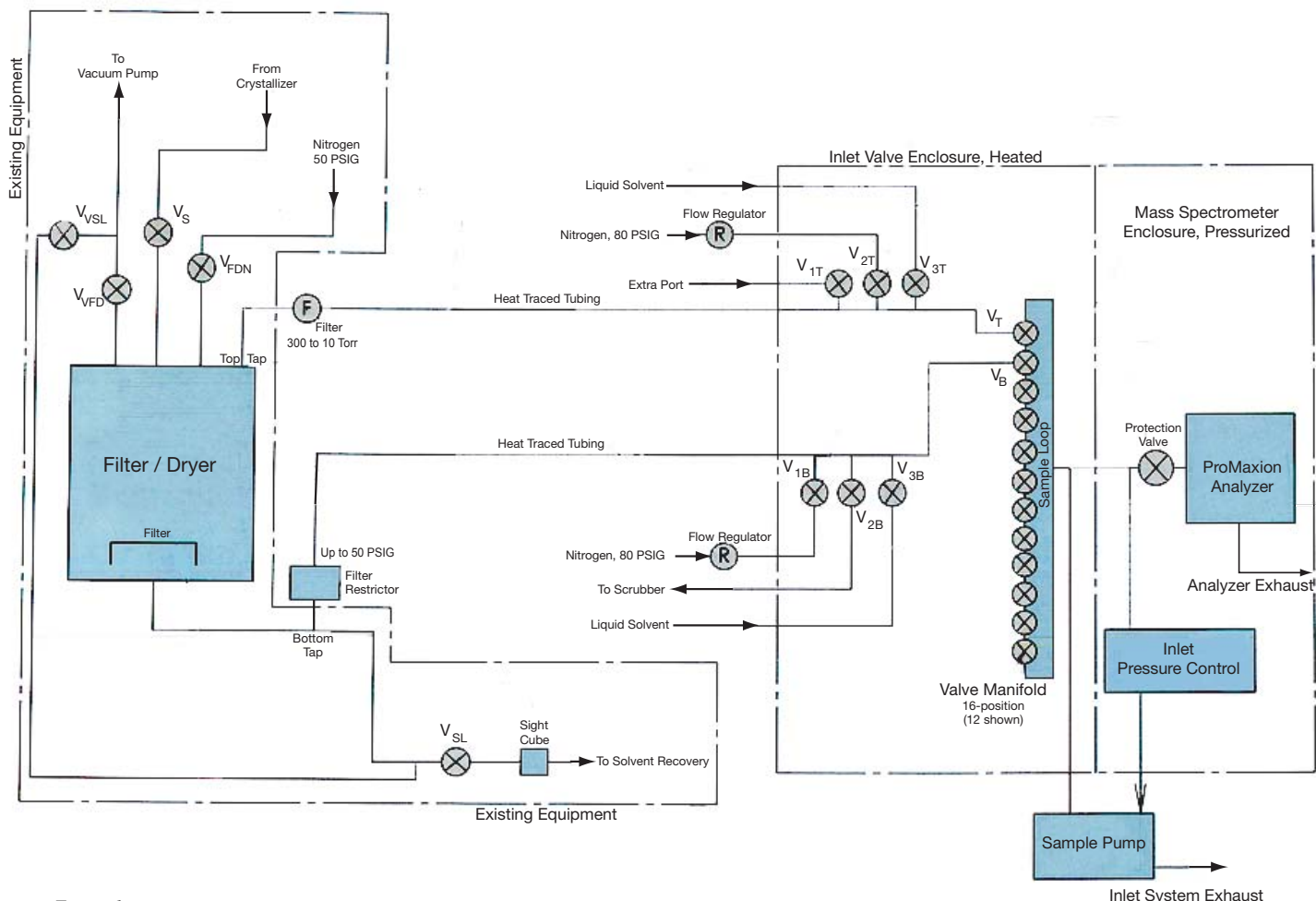


Figure 1.

A typical filter/dryer. Monitoring the solvent profile over time provides the information needed to determine the end point. The analyzer also can measure at the drain outlet to determine when bulk liquid solvent has been removed and it is time to begin vacuum drying. Depending on the dryer application, some or all of the illustrated facilities may be required.

### Process Overview

The vast majority of pharmaceutical intermediates and end products are produced by synthesis, which requires a combination of chemicals, a solvent into which they are mixed, and a reaction process to produce the desired pharmaceutical. The chemicals may be purchased in bulk or manufactured at another part of the plant on site. A common solvent is isopropyl alcohol (IPA), but the pharmaceutical industry uses a vast range of solvents including xylene, methyl bromide, methyl chloride, dimethyl acetamide, and many more. The reaction process includes some combination of heat, cooling and agitation to cause the product to precipitate out of the mix. At the end of this, the chemical stage, the product is laden with solvent which must be extracted before moving to the finishing phase (intermediates) or consumer packaging (end products).

Pharmaceutical solvent drying uses various combinations of heat, pressure, and vacuum to remove solvent from the product. There are two primary means for initial drying of the product: tray dryers and filter dryers.

## Tray Dryers

Tray dryers are room-sized dryers into which product is loaded. They can be operated at pressure or vacuum and either hot or cold, providing a variety of drying strategies that the process engineer can use. The solvent may be pushed (pressure) or pulled (vacuum) out of the product.

## Filter Dryers

Filter dryers consist of a tank into which the slurry of solvent and product is dropped. As the slurry hits the tank, most of the solvent drains out of the dryer and into the solvent recovery system, aided by pressurizing the dryer. A sieve screen just above the drain captures and holds the product. Once it is determined that most of the liquid solvent has drained, the true product drying begins. Like the tray dryers, various combinations of pressure, vacuum, and temperature are used to remove the solvent.

In either case, a determination must be made as to when all of the solvent that can be removed, has been removed, and the product is ready for the next stage.

## Traditional Method with Manual Sampling

The current manual approach to determining when the product is dried involves starting the drying process (which is usually a minimum of 20 hours) and after a preset time, stopping it, manually removing a sample and taking it to the on-site lab for Loss of Drying (LOD) and/or GC analysis. After waiting for the results, the drying process is run for about three more hours. These steps are repeated until the LOD reaches a predetermined value.

Large-scale drying involves thousands of pounds of product and 20 hours of drying time to finish, and the interruption of the process to accommodate manual product analysis adds many hours to the drying cycle. Since all of the solvents present are flammable and/or hazardous to human health, it is also potentially dangerous.

If the need to stop, analyze, and restart the process can be avoided by online detection of the end point, then the efficiency of the drying process can be increased significantly and the risk reduced. This is exactly what the ProMaxion process mass spectrometer can do.

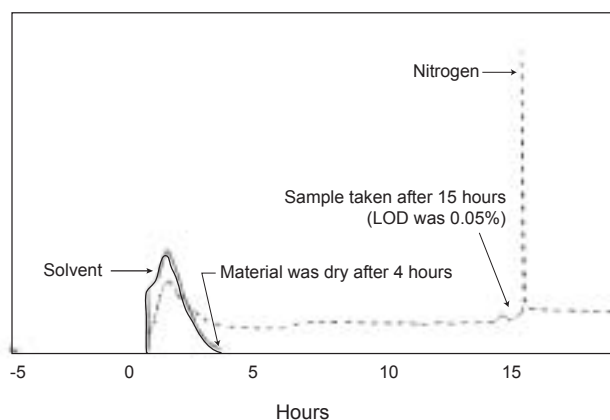


Figure 2.

The solvent concentration in the exhaust gas was monitored through a complete drying cycle. Nitrogen (dotted line) was also recorded to show when the access door of the dryer was opened to obtain a sample for loss on drying (LOD) analysis. It is clear that all of the solvent was removed from the product after about 4 hours, yet with a total drying time of 15 hours, no further drying occurred.

## Fully Automated Method with ProMaxion

Solvent vapors are driven from the product during the pressure or vacuum drying process and can be monitored in the exhaust line of the dryer. It has been determined that the amount of solvent measured in the exhaust line is directly proportional to the amount of solvent remaining in the product<sup>1</sup>.

The ProMaxion will pinpoint, without operator intervention, the moment when the product has been dried as much as is possible. The output from the instrument can be used to control all aspects of the drying cycle from product entry, to its removal for further processing. And, since the ProMaxion can have up to 32 sample inlets, multiple reactors and sample points can be monitored using a single instrument.

The instrument can be set up for different solvents since it is easy to find a unique mass specific to each solvent. This, combined with the real-time response of the ProMaxion, allows one instrument to monitor multiple dryers, each assigned its own configuration. In addition to the solvent, other peaks of interest can be monitored, for example to track air entry into the drying chamber. The mass spectrometer can be used to signal the endpoint of the drying cycle as well as to determine the optimum time to begin vacuum drying after filtration.

Because of the wide range of sample pressures, hazardous area requirements, and the presence of liquids as well as solids in the inlet lines, the sample handling system can vary from simple to very complex. An automatic blow back is required to keep filters and sample lines clean. AMETEK has the experience to design a complete system providing the ability to automate the control of single or multiple dryers.

## Ease of Use and Calibration

The software provides easy set up, operation, and calibration and includes advanced alarm and automation capabilities. Self-diagnostics and modular design ensure ease of maintenance by your own personnel on site, with modem support available for additional factory diagnosis and troubleshooting.

## Benefits

- Reduce drying time significantly
- Determine end point without opening dryer
- Eliminate interrupting the process for LOD product analysis
- Monitor multiple dryers with one analyzer
- Detect abnormal conditions
- Select specific solvent for each dryer
- Purge sample inlet systems with automatic line cleaning
- Works with any combination of pressure or vacuum

<sup>1</sup> David J. am Ende et al., On-Line Monitoring of Vacuum Dryers using Mass Spectrometry, *Organic Process Research & Development*, 2000, 4 (6), 587-593



150 Freeport Road, Pittsburgh, PA 15238 U.S.A. TEL: (412) 828-9040 FAX: (412) 826-0399 <http://www.ametekpi.com>

ProLine Dryer App (03/21/03)

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